

Evaluating HbA1c, BMI and Urinary Biochemistry as Risk Factors for Renal Tract Stones (Urolithiasis)

M. Farrukh Abbas Awan^{1*}, Muhammad Ilyas², Aqsa Malik³, Muhammad Farooq⁴

ABSTRACT

OBJECTIVE: To evaluate the role of HbA1c, BMI and urinary parameters as predictors of renal stone formation.

METHODOLOGY: This case-control study analyzed medical records of 300 patients with renal tract stones and 300 control subjects at the Ahmed Medical Complex in Rawalpindi from January to December 2024. Clinical data included demographics, BMI, HbA1c levels and urinary parameters (pH, citrate, Calcium). Statistical analysis was performed using t-tests, chi-square tests and logistic regression to identify significant predictors.

RESULTS: Patients with urolithiasis had significantly higher BMI ($28.1 \pm 3.6 \text{ kg/m}^2$) and HbA1c ($7.2 \pm 1.4\%$) than controls ($p < 0.001$). Urinary calcium excretion was elevated while citrate levels and urinary pH were lower in patients ($p < 0.001$). Logistic regression identified HbA1c $\geq 6.5\%$ (OR: 2.3, $p < 0.001$) and BMI > 25 (OR: 1.7, $p = 0.002$) as significant predictors. Patients with uric acid stones exhibited higher HbA1c levels than patients with calcium oxalate stones.

CONCLUSION: Metabolic factors, particularly HbA1c and BMI, play a critical role in urolithiasis. Integrating glycemic control and weight management into preventive strategies could reduce the disease burden.

KEYWORDS: Urolithiasis, HbA1c, BMI, Urinary parameters, Renal stones, Lithotripsy, Metabolic factors.

INTRODUCTION

Urolithiasis is highly prevalent in South Asia, attributed to dietary patterns, high temperatures, and metabolic disorders. In Pakistan, the prevalence is estimated at 12%-15%, with calcium oxalate stones being the most common type¹. Similarly, India reports a prevalence of 10–12%, where the burden is exacerbated by inadequate hydration and high dietary oxalate intake². In contrast, Europe and the USA have a lower prevalence of 6–9%, likely reflecting differences in healthcare access, climate and lifestyle factors³. An intermediate prevalence is observed in China, at 8–10%, where dietary factors and genetic predispositions significantly contribute⁴. Despite these regional variations, metabolic abnormalities such as hyperglycemia are increasingly recognized as global contributors to renal stone formation.

Renal tract stones (urolithiasis) pose a significant morbidity and healthcare cost. Their pathogenesis is multifactorial, involving genetic, dietary and metabolic

factors. Among these, metabolic syndrome, particularly insulin resistance and hyperglycemia, has garnered attention for its role in altering urinary biochemistry and promoting lithogenesis. Studies in Europe and the United States have shown that hyperglycemia reduces citrate excretion, a key inhibitor of stone formation³. Similarly, research in China⁴ and India² highlights the role of altered urinary pH and increased calcium excretion in individuals with poor glycemic control. Chronic hyperglycemia alters renal tubular function, promoting crystallization by increasing urinary calcium and oxalate excretion while reducing citrate levels³. The rationale for this study lies in the growing recognition of metabolic factors, including hyperglycemia and obesity, as key contributors to urolithiasis. Investigating the role of these factors can enhance the understanding of stone pathogenesis and inform targeted interventions. We conducted this study to evaluate the role of HbA1c, BMI and urinary parameters as predictors of renal stone formation.

METHODOLOGY

This case-control study analyzed medical records of patients who presented to Ahmed Medical Complex for lithotripsy from January to December 2024. The hospital committee approved the study, and patient confidentiality was maintained through the anonymization of data. Informed consent was waived because this study analyzed medical records, and all procedures complied with the Declaration of Helsinki. The sample size was calculated using the formula: $N = (Z^2 * P * (1-P)) / E^2$, where N represents the required

¹Senior Registrar, Department of Urology, Watim Medical & Dental College, Rawat, Rawalpindi, Pakistan

²Asst. Professor, Department of Medicine, Watim Medical & Dental College, Rawat, Rawalpindi, Pakistan

³Associate Professor, Department of Biochemistry, Watim Medical & Dental College, Rawat, Rawalpindi, Pakistan

⁴Associate Professor, Department of Medicine, Watim Medical & Dental College, Rawat, Rawalpindi, Pakistan

Correspondence: farrukhabbasawan@gmail.com

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sample size, Z is the Z-score, P is the estimated prevalence of the condition, and E is the desired margin of error. Using an estimated prevalence of 40% of urolithiasis,⁵ 25% in controls, a confidence level of 95%, and a margin of error of 5%, the minimum required sample size per Group was 286. To account for potential missing data, 300 participants were included in each Group.

Using a purposive technique, a total of 300 patients with renal tract stones confirmed through imaging were identified as the case group. A total of 300 control subjects were selected from the same clinic during the same study period. The control group consisted of adults of any gender aged 18 years or older who presented to the clinic for reasons unrelated to urological conditions. Exclusion criteria for both groups included individuals with known metabolic disorders, recent urological surgery, pregnancy, lactation, and those on medications affecting Calcium or uric acid metabolism.

Clinical data - including patient demographics, body mass index (BMI), glycated hemoglobin (HbA1c) levels, and stone composition were retrieved and analyzed from hospital medical records. Dietary assessment was based on retrospective extraction of information from clinicians' notes documented in patient charts, where available. These qualitative records included habitual intake patterns of lithogenic dietary components such as oxalate-rich foods (e.g., spinach, tomatoes, chocolate), sodium, animal protein, and fluids (including plain water and carbonated beverages), as recorded by attending clinicians during outpatient visits. Although no validated food-frequency questionnaire or 24-hour dietary recall was administered prospectively, the available documentation was used to estimate nutritional exposures relevant to stone formation. For analytical purposes, dietary intake was categorized into broad risk groups (e.g., high vs low oxalate or sodium intake) based on clinical interpretations recorded in the notes.

For urinary biochemical analysis, documentation confirmed that midstream, clean-catch urine samples were collected from all patients during outpatient visits using sterile containers, in accordance with standard aseptic collection protocols to minimize contamination and ensure specimen integrity. To maintain consistency and obtain optimally concentrated samples, all urine specimens were collected in the early morning (between 7:00 AM and 9:00 AM). Samples were either processed within 1 hour of collection or stored at 4°C and analyzed within 6 hours to prevent degradation. Urinalysis included measurement of pH, citrate excretion, urinary Calcium, and uric acid concentrations using standardized automated analyzers and validated colourimetric assays, according to hospital laboratory SOPs. Internal and external quality controls were used to ensure the reliability and accuracy of test results. For patients who had undergone lithotripsy or stone

extraction, stone composition was evaluated using Fourier-transform infrared (FTIR) spectroscopy, as recorded in the pathology database.

Statistical analysis was performed using SPSS version 25. Continuous variables were expressed as mean $\pm$ standard deviation, and categorical variables were expressed as percentages. Group comparisons were made using independent t-tests for continuous variables and chi-square tests for categorical variables. The association between HbA1c levels and stone formation was assessed using logistic regression, adjusting for potential confounders, including Age, gender, BMI, and dietary habits. A p-value <0.05 was considered statistically significant.

RESULTS

The mean Age of participants in Group I was 45.6 ± 12.3 years, while the mean Age of participants in Group II was 44.8 ± 11.9 years. There was no statistically significant difference in the mean Age between the two groups. In terms of gender distribution, males constituted 60% of Group I and 58% of Group II. This difference was not statistically significant ($p=0.89$). However, the Body Mass Index (BMI) was significantly higher in Group I compared to Group II. (Table I)

Table I:
Demographic characteristics of participants

Variable	Group I (n=300)	Group II (n=300)	p-value
Mean Age (years)	45.6 ± 12.3	44.8 ± 11.9	0.67
BMI (kg/m ²)	28.1 ± 3.6	24.9 ± 2.8	<0.001

Biochemical parameters showed significant differences between the two groups. Group I had a higher mean HbA1c level compared to Group II. Similarly, urinary calcium excretion was elevated in Group I relative to Group II. Urinary citrate levels were lower in Group I. Additionally, the urinary pH was significantly lower in Group I. (Table II)

Table II:
Biochemical characteristics of study participants

Variable	Group I (n=300)	Group II (n=300)	p-value
HbA1c (%)	7.2 ± 1.4	5.8 ± 0.9	<0.001
Urinary Calcium (mmol/day)	8.9 ± 1.2	7.2 ± 1.0	<0.001
Urinary Citrate (mmol/day)	1.2 ± 0.4	2.3 ± 0.5	<0.001
Urinary pH	5.4 ± 0.3	6.2 ± 0.4	<0.001

Logistic regression analysis identified key predictors of stone formation. Participants with an HbA1c level of $\geq 6.5\%$ had an odds ratio (OR) of 2.3 (95% CI: 1.8–2.9; $p<0.001$), suggesting they were more than twice as likely to develop stones compared to those with lower levels. (Figure I) Those with an HbA1c level of $\geq 8.0\%$

had an even higher odds ratio of 3.1 (95% CI: 2.4–4.2; $p < 0.001$). A BMI greater than 25 was also associated with increased risk, with an odds ratio of 1.7 (95% CI: 1.2–2.4; $p = 0.002$). **(Figure 1)**

A subgroup analysis of Group I revealed differences based on stone composition. 65% of cases had calcium oxalate, with a mean HbA1c of $7.0 \pm 1.2\%$, compared with participants with uric acid stones, who had a higher mean HbA1c of $7.8 \pm 1.3\%$. **(Figure 2)**

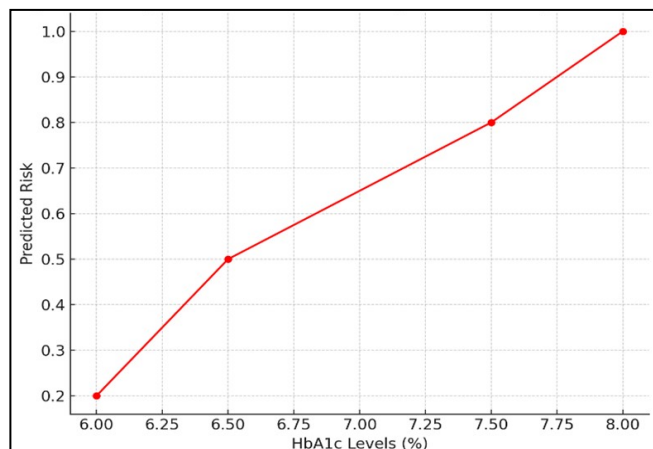


Figure 1: Predicted risk of renal stone formation across HbA1c Levels

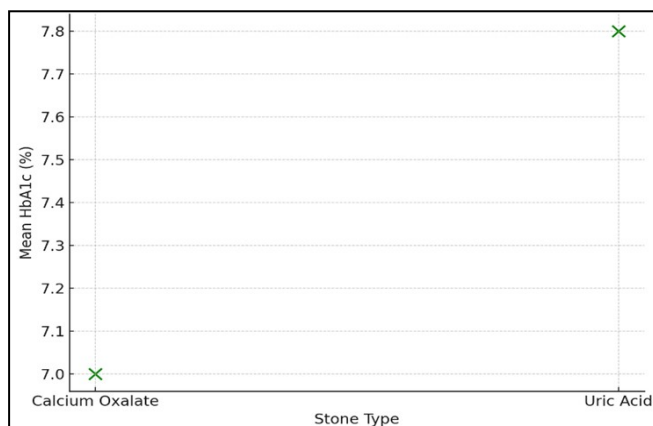


Figure 2: Correlation between HbA1c and stone composition

DISCUSSION

In our study, the gender distribution of urolithiasis cases did not show a statistically significant difference, in contrast with global and regional trends. Many researchers have consistently shown that men exhibit a higher lifetime prevalence of urolithiasis, estimated at up to 14% compared to women, and have suggested that gender-specific metabolic and hormonal differences contribute to this disparity^{6,7}. Men generally have higher urinary concentrations of lithogenic agents such as Calcium, uric acid, and phosphate. In contrast, women have greater urinary citrate excretion, which offers a protective effect against stone formation⁸. Therefore, gender should be considered when evaluating the risk and development

of kidney stones. Despite the absence of statistically significant gender-based differences in our study, we still observed a numerically higher prevalence of urolithiasis among males. This is consistent with findings from Pakistan^{1,5} and Europe⁶. This male predominance may be explained by factors such as differential dietary patterns, hormonal influences (e.g., testosterone's role in increasing lithogenic risk) and occupational factors associated with dehydration. Furthermore, regional dietary habits—particularly the widespread intake of oxalate-rich foods common in South Asia could potentiate stone formation in predisposed individuals⁸. The difference between our findings and the established literature highlights the possibility of region-specific variables, sample selection biases, or limitations in retrospective gender-stratified metabolic profiling, all of which point to a need for further investigation in prospective, multi-centre studies.

In our study, the mean Age of individuals with urolithiasis was 45.6 years, aligning with findings from India⁹ and China¹⁰. This suggests a consistent age distribution across different populations. However, variations may reflect differences in healthcare access and diagnostic capabilities across regions, particularly in low-resource settings¹¹. The Age and gender distribution of our study mirrored reported trends. However, variations may be attributed to differences in healthcare access and dietary habits, such as the high oxalate intake prevalent in South Asia⁷.

In our study, elevated HbA1c levels correlated with altered urinary biochemistry, consistent with observations from Pakistan¹². These findings suggest that interventions to improve glycemic control may reduce the risk of urolithiasis. Integrating metabolic screening into urolithiasis management could enable personalized interventions focused on weight management, dietary counselling, and glycemic control. Further research should prioritize longitudinal studies to confirm causality and explore preventive measures.

We observed significantly higher HbA1c levels in patients with urolithiasis. Elevated HbA1c levels, indicative of poor glycemic control, have been strongly associated with urolithiasis in previous studies from Pakistan¹² and India¹³. Chronic hyperglycemia may alter urinary composition, increasing the risk of calcium oxalate and uric acid stones. Differences in glycemic control trends may be attributed to variations in diabetes prevalence and management practices across regions¹⁴.

We found that elevated BMI emerged as a significant risk factor, consistent with findings from China¹¹ and Europe⁶. This association is likely mediated by obesity-induced insulin resistance, leading to increased urinary calcium excretion and decreased citrate levels. We observed a significant difference in BMI between urolithiasis patients and controls. This finding is consistent with research from China¹¹ and Europe⁶, which identified that elevated BMI was a risk factor for

urolithiasis. Obesity and overweight status contribute to metabolic abnormalities, including insulin resistance, which promotes stone formation through hypercalciuria and reduced urinary citrate. Differences in BMI associations across regions may stem from varying genetic predispositions and lifestyle factors, such as physical activity levels and dietary sodium intake¹⁴.

Urinary calcium levels were significantly elevated in the urolithiasis group. Hypercalciuria is a significant risk factor for calcium stone formation, with similar observations noted in European studies¹⁵. Regional differences in dietary Calcium and vitamin D intake might influence urinary calcium levels¹⁶.

Urinary citrate levels were markedly lower in the urolithiasis group. Citrate acts as an inhibitor of stone formation by chelating Calcium, and hypocitraturia has been highlighted as a key factor in studies from China¹⁷ and Europe⁶. This difference might be linked to dietary acid loads and potassium intake, which vary significantly between Asian and Western diets¹⁸.

Urinary pH was significantly lower in the urolithiasis group. Low urinary pH is a recognized risk factor for uric acid stone formation, corroborated by studies in India² and Pakistan¹. Differences in urinary pH across regions may reflect dietary acid-base balance and hydration habits⁸.

Logistic regression identified HbA1c levels $\geq 6.5\%$ and $\geq 8.0\%$ as significant predictors of stone formation. These results align with research from India¹³, which found that poor glycemic control was a strong predictor of urolithiasis. BMI >25 was also associated with an increased risk, consistent with findings from Europe³. Regional variations may influence differences in the strength of predictors of the prevalence of metabolic syndrome and access to healthcare¹⁴.

Our subgroup analysis revealed differences in stone composition by HbA1c level. Participants with calcium oxalate stones had a higher mean HbA1c. These findings are in line with studies from Pakistan¹² and China¹⁰, which reported metabolic differences influencing stone type. Higher HbA1c levels in patients with uric acid stones emphasize the roles of insulin resistance and acid-base imbalance in their pathogenesis¹⁹. Regional dietary patterns and genetic predispositions may explain differences in stone composition prevalence¹⁶.

This study stands out for its comprehensive approach to investigating risk factors for kidney stone formation. A large sample size provides robust statistical power, enabling a reliable comparison of demographic and biochemical parameters between stone-forming individuals and a control group. The analysis is further strengthened by subgroup analyses that examine the relationship between stone composition and metabolic markers, such as HbA1c, thereby enhancing the study's clinical significance. Ultimately, the application of logistic regression analysis successfully identifies key predictors of kidney stone formation, including

BMI and HbA1c levels, providing valuable insights for the prevention and management of this prevalent health issue. Nevertheless, the study has several limitations. Firstly, the cross-sectional design precludes the establishment of a causal relationship between metabolic factors and kidney stone formation. Secondly, the study did not directly assess potential confounding factors such as dietary intake, fluid consumption, physical activity, and genetic predispositions, which could significantly influence the observed associations. Thirdly, the single-centre design may limit the generalizability of the findings to other populations or regions. Fourthly, the absence of longitudinal data restricts the ability to understand the temporal relationship between metabolic changes and stone formation. Finally, while regional dietary patterns are considered, the lack of direct dietary data on oxalate, sodium, and calcium intake limits a comprehensive understanding of their impact on urinary parameters and subsequent stone risk.

Despite its limitations, our study highlights the crucial role of metabolic factors in the risk of urolithiasis. Integrating BMI and HbA1c into routine assessments enables identification of high-risk individuals, particularly those with poor glycemic control or obesity. This knowledge highlights the importance of lifestyle modifications, including weight management programs and dietary adjustments to reduce sodium intake and intake of oxalate- and acid-forming foods, while increasing intake of citrate-rich foods. Effective diabetes management through medication, diet, and exercise is crucial for reducing the risk of stone formation in this population. Furthermore, individualized interventions are necessary, with uric acid stone formers potentially benefiting from alkalization therapy to address low urinary pH, and calcium oxalate stone formers requiring specific dietary and pharmacological approaches to manage hypercalciuria and hypocitraturia. Given the significant contribution of metabolic risk factors, public health initiatives should prioritize raising awareness of the links among obesity, diabetes, and urolithiasis, implementing screening programs, and promoting preventive measures at the community level to address the burden of this disease effectively.

CONCLUSION

There is a significant association between metabolic factors, such as BMI, HbA1c levels, and urinary composition, and stone formation.

Ethical Permission: Ahmed Medical Complex, Rawalpindi, Pakistan, Ethical exemption letter No. DCA/Amc/25/129.

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on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Awan MFA: Data collection, data analysis

Ilyas M: Interpretation of data

Malik A: Study design and concept

Farooq M: Literature search

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